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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,066	10/12/2001	Kent B. Thudium	16095.002	1828

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EXAMINER

MARVICH, MARIA

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary

Application No.

09/977,066

Applicant(s)

THUDIUM ET AL.

Examiner

Maria B Marvich, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 23-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This office action is in response to an amendment filed 9/22/03. Claims 1-8 and 12-13 have been amended. Claims 1-22 have been cancelled. Claims 23-31 have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in the office action filed 6/17/03 and slightly reworded below.**

Applicants claim a genus of hCMV Intron A fragments comprised sequences having at least 75% sequence identity to contiguous sequences found at positions 1-25 or 1-51 and 775-820 or 741-820 of SEQ ID 1 that can drive expression levels greater (to two-fold, ten-fold or fifty-fold) than that by a control expression cassette without intron A.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical

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and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus. The invention claims as an essential element that the intron A fragment drive expression levels to greater than i.e. two-fold, ten-fold or fifty-fold that of a control construct without the intron A fragment. It is disclosed that a construct containing an intron A fragment from 1-51 and 741-834 increases expression by two-fold over a "parent" vector in *in vitro* assays (figure 5) and less than two-fold in *in vivo* assays (figure 7). The parent is not a control vector without Intron A. However, there is no actual reduction to practice or clear depiction of what structures or properties are required for generation of a intron A fragment or a fragment with 75% identity to the sequences found at positions 1-25 or 1-51 and 775-820 or 741-820 of SEQ ID 1 that can drive expression levels to greater than i.e. two-fold, ten-fold or fifty-fold compared a control without intron A. Neither the instant disclosure nor the prior art provide a correlation between the structures of the recited intron A fragments and their ability to drive expression. Given the diversity of fragments encompassed by the rejected claims and the inability to determine which fragments will also have the essential element of driving expression greater than i.e. two-fold, ten-fold or fifty-fold a control cassette without Intron A, it is concluded that the skilled artisan would not be able to reliably envision those other embodiments capable of satisfying the functional limitations of the claims. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Response to Arguments

Applicants traverse the rejection of claims 1-22 under 35 U.S.C. 112, first paragraph for lack of written description in the amendment filed 9/22/03. Applicants argue that claims 1, 5 and 9-22 have been rejected improperly as “a positive limitation from the specification cannot be read into a claim that does not impose that limitation” and limitations have been impermissibly imported into claims 1, 5 and 9-22. As to remaining claims 2-4 and 6-7, applicants argue that the specification sufficiently provides a description of the invention and relevant identifying characteristics. According to applicants, the Examiner has not provided evidence to dispute that applicant was in possession of the claimed invention at time of filing. As well, the written description as based upon the disclosure and publications submitted at time of filing indicate applicant have complied with written description. Specifically, applicants point to Table 1 and Figure 4, which teaches 11 constructs that exhibited levels of expression that are higher than achieved with the parent construct. As these constructs are not compared to a vector that lack completely Intron A but to a vector that retained the full-length Intron A, applicants state that it is presumed that the expression levels would have been greater than 2-fold, 10-fold and even fifty-fold when actually compared to a vector without Intron A and not to a cassette with full length Intron A. Applicant further draws upon Chapman, page 3984, as evidence of an expectation of these results. Applicants argue that there is no need to exemplify by reduction to practice of every sequence falling within the scope of the claims in order to meet the Written Description requirements. Rather, those sequences that are provided in Figures 1-3 and Table 1 teach the structure. Functional characteristics amount to increased expression coupled with known and disclosed correlation between structure and function. Again applicant refers to

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Chapman et al, which teaches that plasmids with Intron A “out-perform” plasmids without Intron A. As well, the specification teaches the regions of Intron A, contemplated for deletion or change. Applicants state that these disclosures are found on pages 8, line 18 through page 9, line 14, page 9-10 bridging paragraph, page 17, line 6 through page 18, line 13, pages 19-10 (sic 20), bridging paragraph.

The arguments filed 9/22/03 have been considered but are not persuasive. Reasons to dispute that applicants have met the Written Description Requirement were provided in the Office action filed 6/17/03. They have been restated in this office action. Claims 1-22 recite a broad genus of human cytomegalovirus (hCMV) Intron A fragments lacking at least 10 internal nucleotides and comprising nucleotides having at least 75% sequence identity to nucleotides at positions 1-25 and to nucleotides at positions 775-820. It is further recited that the fragments must direct the transcription of a coding sequence to levels greater than (i.e. 2-fold, 10-fold, 50-fold) those levels achieved by a corresponding construct that completely lacks an Intron A sequence. In the specification, fragments that comprise nucleotides found at positions 1-25 and 775-820 are alone disclosed as members of this class of proteins. While the specification has characterized this specific member as to the ability of these fragments to direct expression as compared to a control vector (see figure 3-4), it has not characterized the broad genus of Intron A fragments. Furthermore, applicants have not demonstrated that any of the fragments direct the transcription of a coding sequence to levels greater than those levels achieved by a corresponding construct that completely lacks an Intron A sequence. While applicants argue that it would be presumed by the skilled artisan that fragments that direct expression of a coding sequence to levels greater than the full intron, there is no evidence to indicate this is true. In fact, given that a

deletion in the Intron A fragment leads to level of expression that are greater than a full length fragment, a skilled artisan could also conclude that a construct with further deletions would lead to even greater levels of transactivation such that the levels of expression from a construct without Intron A would be greater than those of the instant invention. The sections of the specification cited by applicants as support for the written description of the claimed invention teach use of Intron A fragments that are comprised of sequences from 1-25 and 775-820 of Intron A. Therefore, the disclosure of pCON3 and fragments comprised of the nucleotides in pCON3 and its ability to direct expression to levels 2-fold greater than a vector with full length Intron A do not constitute written description for the identification of any Intron A fragments lacking at least 10 internal nucleotides and comprising nucleotides having at least 75% sequence identity to nucleotides at positions 1-25 and to nucleotides at positions 775-820. Furthermore, the specification lacks disclosure as to the relevant identifying characteristics of a Intron A fragments lacking at least 10 internal nucleotides and comprising nucleotides having at least 75% sequence identity to nucleotides at positions 1-25 and to nucleotides at positions 775-820 that would be able to direct expression of a coding sequence to levels greater than that of a vector without Intron A. The fragment of Chapman et al by applicants own admission in the amendment filed 9/22/03 does not represent fragments of the instantly claimed invention.

Given the diversity of sequences that are should be related by at least 75% to nucleotides at positions 1-25 and to nucleotides at positions 775-820 and the uncertainty that a sequence related by 75% will be effective at driving expression to levels greater than a control vector, it must be considered that any Intron A fragment of the genus claimed must be empirically determined. In an unpredictable art, the disclosure of one example in one genus would not

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represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus

Conclusion

No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucell, PhD can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and 1 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Kay Pinkney, patent analyst, whose telephone number is (703) 308-0196.

Maria B Marvich, PhD
Examiner
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December 16, 2003


GERRY LEFFERS
PRIMARY EXAMINER